BASF Aktiengesellschaft

BASF

BASF Aktiengesellschaft · 67056 Ludwigshafen

Food and Drug Administration
Dockets Management Branch
HFA-305
Room 1061
5630 Fishers Lane
Rockville, Maryland 20852

April 15, 1999/Ri Dokument10

ME/DZ - D 205
Dr. Reinhardt
☎ ++621-60-9 36 74
🖷 ++621-60-9 29 30

Dear Sir or Madam:

BASF expressly authorizes the release of the attached materials contained in the submission dated April 12, 1999 to public Docket Nos. 78N-0038 CP2 and 78N-0038 CP7.

If you have any questions concerning the above authorization, please contact Ms. Kathleen M. Sanzo, Morgan, Lewis & Bockius LLP., Washington, D.C., (202) 467-7209.

Sincerely,

BASF Aktiengesellschaft
Regulatory Affairs Fine Chemicals

Dr. Rolf-Dieter Reinhardt

1800 M Street, N.W.
Washington, D.C. 20036-5869
202-467-7000
Fax: 202-467-7176

Morgan, Lewis
& Bockius LLP
COUNSELORS AT LAW

Kathleen M. Sanzo
202-467-7209

April 9, 1999

BY HAND DELIVERY

Food and Drug Administration
Dockets Management Branch
HFA-305
Room 1061
5630 Fishers Lane
Rockville, Maryland 20852

CONFIDENTIAL: CONTAINS CONFIDENTIAL COMMERCIAL INFORMATION—NOT FOR PUBLIC RELEASE

Re: Data and Information Concerning PEG-25 PABA (Univul P 25) (Docket No. 78N-0038 CP2) and Octyl Triazone (Univul T 150) (Docket No. 78N-0038 CP7) Safety Data

Dear Sir or Madam:

In connection with BASF AG's May 25, 1989 petition to FDA to reopen the administrative record in the over-the-counter Sunscreen Drug Products Monograph to consider including ethoxylated ethyl-4-aminobenzoate (Univul P 25, INCI: PEG-25 PABA) as a Category I generally recognized as safe and effective sunscreen ingredient,[1/] and BASF AG's November 15, 1996 request that the administrative record be reopened to consider inclusion of octyl triazone[2/] (Univul T 150, INCI: Octyl Triazone) as a Category I generally recognized as safe and effective sunscreen ingredient, please find enclosed for your consideration an original and three copies of supplementary safety data concerning PEG-25 PABA and information concerning the final listing of Octyl Triazone in the European Union. The data are intended to further support the aforementioned Citizen Petitions and written request to consider inclusion of PEG-25 PABA and Octyl Triazone as Category I safe and effective sunscreen active

---

1/ Citizen Petition from BASF to FDA (May 25, 1989) (Docket No. 78N-0038 CP2).

2/ Citizen Petition from BASF to FDA (November 15, 1996) (Docket No. 78N-0038 CP7).

78N-0038 Sup 23

ingredients based on their long and safe marketing history in the European Union. These enclosed tests include:

- **Phototoxicity/Photosensitization**: Evaluation of the photoallergic potential of PEG-25 PABA was performed in the albino Hartley guinea-pig, according to a protocol using 30 animals of both sexes, allocated to one control group of 10 animals, one experiment group of 10 animals, and one positive control group of 10 animals. The animals were given four intradermal injections of Freund's complete adjuvant at 50% (V/V) and topical application of the test substance, followed by irradiation at the dose levels for UVA and UVB. PEG-25 PABA did not provoke any phototoxic or photosensitive reaction in the experimental animals.

- **Photomutagenicity in E. Coli**: PEG-25 PABA was assayed for an ability to induce mutation in *Escherichia coli* strain WP2, following exposure to a range of doses of UVA and UVB light, in 2 separate experiments. The data obtained gave no indication of an ability of the test chemical to induce mutation following photoactivation.

- **Photomutagenicity in CHO Cells**: In this study, the treatment of cultures with concentrations up to 5000 μg/ml PEG-25 PABA in the presence of either 200 mJ/cm^2 UVA, 38 mJ/cm^2 UVB (unfiltered) or 700 mJ/cm^2 UVA (glass-filtered) did not show significant increase in the incidence of chromosome aberrations in CHO cells, when compared with concurrent controls. PEG-25 PABA was tested for toxicity in CHO cells in a range-finder experiment using final concentrations at 78.12, 156.2, 312.5, 625, 1250, 2500, and 5000 μg/ml. No mitotic inhibition or precipitation of PEG-25 PABA were observed and 5000 μg/ml was selected as the top dose for the main study. PEG-25 PABA was found not to be photoactivated to a clastogenic form detectable in this assay.

- ***In Vitro* Chromosome Aberration Assay in V 79 Cells**: PEG-25 PABA was assessed for its potential to induce structural and/or numerical chromosomal aberrations in Chinese hamster V 79 cells *in vitro* both in the presence and absence of a metabolizing system. PEG-25 PABA was found to be neither a

chromosome-damaging (clastogenic) agent nor to have an aneugenic activity in V 79 cells *in vitro* under the conditions of the experiments implemented.

- ***In Vitro* Percutaneous Penetration Through Human Skin**: The potential for skin penetration of PEG-25 PABA was evaluated *in vitro* following a single application of 10% aqueous solution to human epidermis from a biopsy specimen. A static skin penetration chamber design was used in this study. It was found that PEG-25 PABA has the potential to penetrate human epidermis with the maximal absorption rate obtained within 2 hours post-application. Thereafter, the flux declines and reaches a steady-state at approximately 8 hours post-application.

FDA's regulations permit the Agency to rely on foreign data in support of the safety and efficacy of new prescription drugs,[3/] and the FDA has stated its intent to propose regulations expressly permitting the use of foreign data for inclusion of a product in an OTC monograph.[4/] Therefore, it is clear from the proposal that FDA recognizes the acceptability of foreign marketing data as support for the safety, efficacy and material extent and time of use of OTC pharmaceuticals.

In view of the long and safe use in Europe and elsewhere, marketing history, and available data supporting the safety and efficacy of PEG-25 PABA and Octyl Triazone, the statutory, regulatory and practical requirements for inclusion of these ingredients in the OTC monograph review process are satisfied, and the Agency should promptly grant the related pending petitions concerning these ingredients and permit their inclusion in the OTC sunscreen monograph.

As with other ingredients in the OTC review process, it would then be deemed permissible for BASF to market PEG-25 PABA and Octyl Triazone in the U.S. pending promulgation of a final OTC monograph for sunscreen ingredients, in which the ingredients are determined to be, as BASF believes warranted, in Category I for safety and efficacy for sunscreen products. Interim marketing is especially appropriate in view of the extraordinarily long time which

---

3/ See 21 C.F.R. § 314.106 (1995).

4/ 61 Fed. Reg. 51,625 (Oct. 3, 1996).

FDA has taken to review BASF's petitions, and the significant public health need for alternative sunscreen products in the U.S. market.

All of the enclosed materials marked "confidential" are confidential commercial or financial information relating to test data and market information that has not been disclosed to any member of the public, and are not available for public disclosure.

If you have any questions concerning these studies or their results, please contact me. We look forward to the Agency's prompt determination concerning interim marketing of, and the inclusion in the OTC sunscreen products monograph of, PEG-25 PABA and Octyl Triazone.

Sincerely,

Kathleen M. Sanzo

Kathleen M. Sanzo

KMS/hmb

Enclosures

cc: Dr. Rolf-Dieter Reinhardt
Bob Pinko